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AUDLEY A. CIAMPORCERO JR.
JOHNSON & JOHNSON
ONE JOHNSON & JOHNSON PLAZA
NEW BRUNSWICK, NJ 08933-7003

EXAMINER
JAGOE, DONNA A

ART UNIT	PAPER NUMBER
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/081,606	Applicant(s) PLATA-SALAMAN ET AL.	
	Examiner Donna Jagoe	Art Unit 1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-17 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-17 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6,8 .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other:

DETAILED ACTION

Claims 1-17 are presented for examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claims 1-17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of the symptoms of bipolar disorder in a subject, it does not reasonably provide enablement for preventing bipolar disorder. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, predictability of the prior art, state of the prior art and the amount of experimentation necessary. All of the **Wands factors** have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the Invention: Claim 1 is drawn to a method of **preventing** or treating bipolar disorder comprising administering to a subject in need thereof an effective amounts of an enantiomer of formula (I) or enantiomeric mixture wherein one enantiomer of formula (I) predominates. The nature of the invention is extremely

complex in that it encompasses the actual prevention of a bipolar disorder such that the subject treated with above formula does not contract bipolar disorder.

Breath of the Claims: The complex of nature of the claim is greatly exacerbated by breath of the claim. The claims encompass prevention of a disorder whose cause is unknown (Current evidence indicates that, as with other psychiatric disorders, both genetic and environmental factors are thought to contribute to the development of the disorder, and the symptoms that govern the function of neurotransmitters such as serotonin and dopamine are involved in the pathophysiology of bipolar disorder. Additionally, disturbances in the neurotransmission of GABA have also been implicated in the pathophysiology of bipolar illness [Cognos study, page 1, listed as document AO from IDS in paper number 8 dated 14 April 2003). Each of these defects may or may not be addressed by the administration of the claimed compounds.

Guidance of the Specification: The guidance given by the specification as to how one would administer the claimed compounds to a subject in order to actually prevent bipolar disorder is minimal. All of the guidance provided by the specification is directed towards treatment rather than prevention of bipolar disorder.

Working Examples: All of the working examples provided by the specification are directed toward the treatment of a hippocampal kindled rat model, implanted with bipolar electrodes. Evaluation of Formula (I) was made on the basis of suppression of the seizure threshold in the rat model. There is no other data.

State of the Art: While the state of the art is relatively high with regard to **treatment of the symptoms** of bipolar disorders, the state of the art with regard to **prevention** of such disorders is underdeveloped. In particular, there do not appear to be any examples or teachings in the prior art wherein a compound similar to the claimed compounds was administered to a subject to **prevent** development of a bipolar disorder.

Predictability of the Art: The lack of significant guidance from the specification or prior art with regard to the actual **prevention** of a bipolar disorder in a subject with the claimed compounds makes practicing the claimed invention unpredictable in terms of prevention of a bipolar disorder.

The amount of Experimentation Necessary: In order to practice claimed invention, one of skilled in the art would have to first envision a combination of appropriate pharmaceutical carrier, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model system for one of the claimed compounds and test the combination in the model system to determine

whether or not the combination is effective for prevention of bipolar disorder. If unsuccessful, which is likely given the lack of significant guidance from the specification or prior art regard prevention of bipolar disorder with any compound, one of skill in the art would have to then either envision a modification of the first combination of pharmaceutical compound, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model system, or envision an entirely new combination of the above, and test the system again. If again unsuccessful, which is likely given the lack of significant guidance form the specification of prior art regarding prevention of bipolar disorder with any compound, the entire, unpredictable process would have to be repeated until successful. Therefore, it would require undue, unpredictable experimentation to practice the claimed invention to prevent the development of a bipolar disorder in a subject by administration of one of the claimed compounds.

Therefore, a method of **preventing** a bipolar disorder in a subject comprising administering the pharmaceutical composition of formula (I) is not considered to be enabled by the instant specification.

2. Claims 1-17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of **the symptoms** of a bipolar disorder in a subject, it does not reasonably provide enablement for treating a bipolar disorder. The specification does not enable any person skilled in the art to which it pertains, or

with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, predictability of the prior art, state of the prior art and the amount of experimentation necessary. All of the **Wands factors** have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the Invention: Claim 1 is drawn to a method of **preventing** or treating bipolar disorder comprising administering to a subject in need thereof an effective amounts of an enantiomer of formula (I) or enantiomeric mixture wherein one enantiomer of formula (I) predominates. The nature of the invention is extremely complex in that it encompasses treatment of a bipolar disorder, which has many phases such as depression, euphoric mania, dysphoric mania and mixed state.

Breath of the Claims: The complex of nature of the claim is greatly exacerbated by breath of the claim. The claims encompass treatment of a disorder whose cause is unknown and has many phases (current evidence indicates that, as with other psychiatric disorders, both genetic and environmental factors are thought to contribute to the development of the disorder, and the symptoms that govern the function of neurotransmitters such as serotonin and dopamine are involved in the pathophysiology of bipolar disorder. Additionally, disturbances in the

neurotransmission of GABA has also been implicated in the pathophysiology of bipolar illness [Cognos study, page 1, listed as document AO from IDS in paper number 8 dated 14 April 2003). Each of these defects may or may not be addressed by the administration of the claimed compounds.

Guidance of the Specification: The guidance given by the specification as to what type of treatment is being received by administration of the claimed formula (I) for bipolar disorder is minimal. All of the guidance provided by the specification is directed towards treatment but it is not known whether it acts as a mood stabilizer, an anti-depressant or a sedative/hypnotic.

Working Examples: All of the working examples provided by the specification are directed toward the treatment of a hippocampal kindled rat model, implanted with bipolar electrodes. Evaluation of Formula (I) was made on the basis of suppression of the seizure threshold in the rat model. There is no other data.

State of the Art: While the state of the art is relatively high with regard to **treatment of the symptoms** of bipolar disorders, i.e., mood stabilizers, anti-depressants and sedative/hypnotics, the state of the art with regard to **a generic treatment** of such disorders is underdeveloped.

Predictability of the Art: The lack of significant guidance from the specification or prior art with regard to the treatment of a bipolar disorder in a subject with the claimed compounds makes practicing the claimed invention unpredictable in terms of generic treatment of a bipolar disorder.

The amount of Experimentation Necessary: In order to practice claimed invention, one of skilled in the art would have to first envision a combination of appropriate pharmaceutical carrier, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model system for one of the claimed compounds and test the combination in the model system to determine whether or not the combination is effective for treatment of a bipolar disorder. If unsuccessful, which is likely given the lack of significant guidance from the specification or prior art with regard to the generic treatment of a bipolar disorder with any compound except mood stabilizers, one of skill in the art would have to then either envision a modification of the first combination of pharmaceutical compound, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model system, or envision an entirely new combination of the above, and test the system again. If again unsuccessful, which is likely given the lack of significant guidance form the specification of prior art regarding generic treatment of a bipolar disorder with any compound, except mood stabilizers, the entire, unpredictable process would have to be repeated until successful. Therefore, it would require undue, unpredictable experimentation to

practice the claimed invention to prevent the development of a bipolar disorder in a subject by administration of one of the claimed compounds.

Therefore, a method of **treatment of** a subject having a bipolar disorder comprising administering the pharmaceutical composition of formula (I) is not considered to be enabled by the instant specification.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Choi et al. U.S. Patent No. 6,103,759 (reference AA from IDS dated 14 April 2003) in view of Post et al. (reference AS from IDS dated 14 April 2003).

The claims are drawn to a method of preventing or treating bipolar disorder comprising administering to a subject in need thereof an effective amounts of an enantiomer of formula (I) or enantiomeric mixture wherein one enantiomer of formula (I) predominates. Several types of bipolar disorders are recited in instant claim 14 and the dose recited is from about 0.01 mg/Kg/dose to about 100 mg/Kg/dose. Additional claims are drawn to slowing the progression of the disorder by administering the composition of formula (I).

Choi et al. teach the compositions instantly claimed (see entire document) including the enantiomeric mixtures (see claims 1-6) for the purpose of central nervous system disorders (claims 7-12) and especially for anticonvulsive or anti-epileptic treatment (see abstract).

It does not teach treatment of bipolar disorder.

It does not teach the specific doses recited in instant claims 15 and 17.

Post et al. teach that anticonvulsants have moved into an important position as alternatives and adjuncts to lithium in the treatment of bipolar illness (see abstract).

Post et al. teach that a series of anticonvulsant agents have emerged as mood stabilizers in patients with bipolar disorder, such as carbmazepine, valpromide, sodium valproate, divalproex sodium, lamotrigine and gabapentin (see entire document, especially conclusion, page 163).

It does not teach the carbamate compositions of formula (I).

It would have been obvious to treat the symptoms of a bipolar disorder with the composition of formula (I) motivated by the teachings of Choi et al. who teach the compositions to be employed for central nervous system disorders, especially as anticonvulsants and the teachings of Post et al. that anticonvulsants are employed in the treatment of bipolar disorders as mood stabilizers.

Regarding the recited doses, as anyone of ordinary skill in the art will appreciate, preferred dosages are merely exemplary and serve as useful guideposts for the physician. The specific safe and effective amount will be vary, with such factors as the particular condition being treated, the severity of the illness of the patient, the duration of treatment, the nature of the concurrent therapy (if any), the specific dosage form to be used, the carrier employed, the solubility of the formula therein and the dosage regimen desired for the composition. Furthermore, it is routine during animal and clinical studies to dramatically vary dosage to obtain data on parameters such as toxicity. For these and other self-evident reasons, it would have been obvious to administer the doses recited instantly motivated by the teaching of Choi et al. and Post et al. above.

Thus the claims fail to patentably distinguish over the state of the art as represented by the cited references.

No claims are allowed.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Donna Jagoe whose telephone number is (703) 306-5826. The examiner can normally be reached on Monday through Friday from 8:00 A.M. - 4:30 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel can be reached on (703) 308-4725. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Donna Jagoe
Patent Examiner
Art Unit 1614

Frederick Krass
Primary Examiner
Art Unit 1614